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LICATLA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/044,722	DICICCO-BLOOM ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-49* is/are pending in the application.

4a) Of the above claim(s) *47-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *47-49* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11 June 2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks filed 21 January 2005 have been entered. Claims 46 – 49 are pending in the instant office action.

Election/Restrictions

2. Applicant's election with traverse of Group II in the reply filed on 21 January 2005 is acknowledged. The traversal is on the ground(s) that the examiner's restriction requirement is improper for the following reasons:

a) The restriction within individual claims is improper as a matter of law.

b) No additional search burden would be presented to the examiner if Groups IV and V were rejoined.

Applicant's traversal is successful, in part, for the reasons enumerated below.

a) Applicant cites *in re Harnish* and *ex parte Hozumi* as suggesting that the restriction is improper, and that applicant may claim his invention in any way he chooses. This reasoning is persuasive. Claims will be examined in their full generic scope. Groups I and II (i.e. claim 46) are rejoined.

b) Applicant argues that no additional search burden would be presented to the examiner if Groups IV and V were to be rejoined. This logic is persuasive, but since applicant elected Group II, the argument is not applicable to Groups IV and V. As the examiner is convinced that no additional search burden would be presented by rejoining *in vivo* and *in vitro* methods together, Groups I and II are rejoined as detailed above.

Applicant also cites MPEP § 803.02 as relevant to the restriction requirement. However, that section relates to Markush groups, specifically whether or not compounds in a Markush group share unity of invention. Since no pending claim includes a Markush group, it is not immediately obvious how this section is relevant.

Restriction between rejoined groups I and II and groups III – VII is still deemed proper for the following reasons:

The methods of rejoined Groups I and II require a PAC1 ligand. It is acknowledged that claim 48 (i.e. Groups VI and VII) also requies a PAC1 ligand. Restriction between claims 46 and 48 is proper because the recited methods require different steps and because the method of claim 48 is to be practiced on a specific patient population. The method of claim 46

comprises the steps of contacting a neuronal precursor cell with a PAC1 ligand. The method of claim 48 requires administering a PAC1 ligand to a patient with a medical condition. Consideration of claim 48 would require search of a vast array of medical conditions, as the claim is drawn to treatment of any medical condition. Search of medical conditions is not required for consideration of claim 46, therefore consideration of claim 48 along with claim 46 would present a serious search burden for the office. Thus restriction between rejoined Groups I and II on the one hand and Groups VI and VII is proper.

The methods of rejoined Groups I and II require a PAC1 ligand. The methods of claim 47 (i.e. Groups III – V) do not require a PAC1 ligand, but rather require a compound which decreases the expression or amount of PACAP in the cell. Compounds that meet this description do not have to be capable of binding the PAC1 receptor. As mentioned on page 4, lines 3 – 4 of the restriction requirement mailed 21 December 2004, the art indicates that forskolin decreases the amount of PACAP mRNA. Forskolin is a stimulator of cyclic AMP but is neither a PACAP antagonist nor a PAC1 ligand. The starting materials required for the methods of Groups III – V cannot be used in the methods of rejoined Groups I and II. Thus the inventions are not related. Furthermore, a search of the patent and non-patent literature for methods of decreasing the expression or amount of PACAP would not be expected to be co-extensive with searches for ligands of PAC1. Therefore consideration of Groups III – V along with rejoined Groups I and II would require an additional search. Restriction between rejoined Groups I and II and III – V is proper.

The methods of rejoined Groups I and II require a PAC1 ligand. The methods of claim 49 (i.e. Group VI) do not require a PAC1 ligand, but rather require a PACAP antagonist, which is not required for the methods of rejoined Groups I and II. For example, anti-PACAP antibodies would be expected to act as PACAP antagonists, as they bind to PACAP and therefore will inhibit its action. Anti-PACAP antibodies would not be expected to bind to PAC1, and therefore are not PAC1 ligands. Because the methods of claims 46 and 49 require different starting materials, they are unrelated inventions. The methods of claim 49 require administering PACAP antagonists to patients in need thereof. Therefore, consideration of this claim would require determining which patient population is the relevant one, and then searching the patent and non-patent literature to determine if methods of increasing brain growth in said patients are in fact novel and non-obvious. Search the literature to determine whether or not PAC1 ligands modulate the growth of neuronal precursor cells would not be expected to encompass the

material that would be searched for claim 49. Therefore, consideration of claims 46 and 49 together would require an additional search, and present a serious burden for the office.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 47 – 49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 21 January 2005. Claim 46 is under examination in the instant office action.

Information Disclosure Statement

4. The information disclosure statement filed 11 June 2002 has been considered. References AG and AH have not been considered as no copy is in the case. Note that only the table of contents of reference AO by Creighton has been considered, as that is all applicant provided. Similarly, only the table of contents, preface, and index have been considered for reference AS by Harlow.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 46 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increases in proliferation of neuronal precursor cells expressing PAC1 receptors in the forebrain following administration of PAC1 receptor antagonists $PACAP_{6-38}$, max.d.4, as well as antibodies against PACAP (specification, p. 6, lines 1 – 2, and p. 9, lines 1 – 6) and decreases in proliferation of same following administration of the PAC1 agonists PACAP (Example 3, p. 27), maxadilan, PACAP27, and VIP (p. 6, lines 2 – 4), does not reasonably provide enablement for increases in proliferation either cerebellum or sympathetic neuroblasts following administration of PAC1 antagonists, or decreases in proliferation in those regions following administration of PAC1 agonists. Furthermore, the specification does not reasonably provide enablement for those "ligands", as recited in the claim, which encompasses agents

which bind to the PAC1 receptor but are neither agonists nor antagonists, nor to modulating the growth of neuronal precursor cells which do not express PAC1 receptors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claim is drawn to a method of modulating growth of neuronal precursor cells by administering an agent that binds to a PAC1. The specification discloses the use of several PAC1 agonists and antagonists and reveals that administration of them lead to decreases and increases, respectively, in incorporation of markers of cell division by neuronal precursor cells in the ventricular zone and cortical plate. The prior art teaches that whether PACAP acts to promote cell division depends on the types of cells being studied. For example, Lu et al. (1998, reference AY on the information disclosure statement) teach that activating PAC1 *increases* neurogenesis in sympathetic neuroblasts (see particularly p. 652, second column), and Vaudry et al. (1999. PNAS 96:9415-9420) teach that PACAP induces mitgoenesis in cerebellar neuronal precursors both *in vivo* (p. 9416, second paragraph of RESULTS) and *in vitro* (p. 9416, first paragraph of RESULTS). Lu et al. hypothesize that 'receptor diversity *may* be *one* mechanism' which determines whether PACAP acts as a mitogen or not (p. 657, first paragraph, emphasis added). However, it is not clear this is the determining factor and furthermore the specification does not disclose which cell types express which receptor isoform. Furthermore Spengler et al. (reference BK on the information disclosure statement) show that some isoforms of the PAC1 receptor pass considerably less current than others and therefore would not be expected to work (see particularly p. 174, Figure 3). Claim 46 is drawn to a method of modulating the growth of neuronal precursor cells, which entails either an increase or a decrease in growth, by administering a PAC1 ligand. But since the effects of PAC1 ligands on the growth of neuronal precursor cells is unpredictable, a skilled artisan would have to resort to undue experimentation to practice the invention as claimed. While broad claims can include some inoperable embodiments, MPEP § 2164.08(b) says that

> claims reading on significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971).

Because PACAP can have opposite effects and the mechanism underlying whether it serves to increase or attenuate cell proliferation are neither well-understood nor disclosed in the

specification, a skilled artisan would not know whether to give a PAC1 receptor ligand that acts as an agonist or as an antagonist to promote proliferation of neuronal precursor cells. Therefore it would not be possible to practice the method of claim 46.

Furthermore, claim 46 is drawn PAC1 ligands, without any requirement that the ligands have a particular effect. Applicant has not explicitly defined ligands in the specification, therefore the examiner has construed this term to include receptor agonists and antagonists, as well as antibodies and any compound that binds to any part of the PAC1 receptor. Not all ligands would be expected to act as either an agonist or an antagonist. For example, ligands which bind PAC1 other than at the PACAP-binding site (e.g. an antibody raised against one of the transmembrane domains) would not be expected to have either a mitogenic or anti-mitogenic effect. The specification is not enabled for PAC1 ligands which are neither agonists nor antagonists.

The claim is drawn to methods of modulating neuronal precursor cell growth by administering compounds which bind to PAC1. The claim encompasses cells which do not express PAC1 receptors, and the prior art teaches that only 64% of neuronal precursors in culture express PAC1 receptors (DiCicco-Bloom et al., Ann NY Acad Sci 865:274-289, see particularly p. 283). Because the specification discloses that the mitogenic and anti-mitogenic effects of PAC1 receptor agonists and antagonists are due to the effects of same on the ligand/receptor system (see p. 6, for example), one of skill in the art would conclude that the receptor is necessary for the ligands to have their effect. Yet the claim does not direct the artisan to cells which express the PAC1 receptor, and clearly not all neuronal precursors express PAC1.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

The nature of the invention, modulating the growth of neuronal precursor cells, is complex. The prior art indicates that using PAC1 receptor ligands to do so is unpredictable and requires the receptor be present. The claims, which are not limited by cell type or chemical

structure, are broad. The claim is akin to a single means claim, i.e., where a means recitation does not appear in combination with another recited element of means and is subject to an undue breadth rejection under 35 USC 112, first paragraph because the specification at most would only disclose those means known to the inventor at the time of the invention, see in particular MPEP 2164.08(a). The working examples are all drawn to forebrain tissue, whereas the claim encompasses all neuronal precursor cells. Therefore, it would require undue experimentation on the part of a skilled artisan to make and use the invention commensurate in scope with the claims.

7. Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claim is drawn to a method of modulating the growth of a neuronal precursor cell by administering ligands of the PAC1 receptor. The claim includes functional language only, and does not include any structural limitations. As noted above, the term "ligand" has not been defined by applicant, and thus can be construed to include any and all compounds which bind to the receptor. "Agonist" and "antagonist" are defined on p. 18 of the specification, but are not limited by structure, and furthermore not all ligands are antagonists or agonists, and not all antagonists and agonists are ligands. For example, QIAexpress Detection and Assay handbook (pp. 55 and 59) teaches that nonspecific cell epitopes can be blocked by proteins including BSA. There is no evidence that BSA is either an agonist or antagonist, but it appears to be able to bind to all proteins. The instant disclosure of three agonists and two antagonists of the PAC1 receptor on p. 6 of the specification does not adequately support the scope of the claimed genus "ligands", which encompasses a substantial variety of subgenera including, for example, small organic molecules and proteins. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614,

1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

Clearly applicant has not described all ligands encompassed by the broad language in the claims.

8. Claim 46 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The scope of the claims and specification as originally filed was drawn to agonists and antagonists of the PAC1 receptor. Claim 46 does not recite agonists and antagonists, but rather recites "ligands". As detailed in the preceding paragraphs, ligands encompass a different scope of compounds than either agonists or antagonists. Ligands include reagents which bind to a target molecule but are neither agonists nor antagonists. Agonists and antagonists do not necessarily have to bind to a receptor in order to exert their effect. For example, an antibody raised against PACAP will bind the PACAP (the ligand), thereby preventing it from exerting its effect on the PAC1 receptor. Anti-PACAP antibodies are clearly PAC1 antagonists because they decrease the activity mediated by the PAC1 receptor and therefore meet the definition of antagonists provided on p. 18 of the specification, yet anti-PACAP antibodies are not PAC1 ligands.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "a pituitary adenylate cyclase activating polypeptide receptor, PAC1,". It is unclear whether applicant is attempting to claim methods of modulating cell physiology using ligands of *any* PACAP receptor, or by using ligands of the PAC1 receptor.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

12. Claim 46 is rejected under 35 U.S.C. 102(a) as being anticipated by Nicot et al. (2000. Society for Neuroscience Abstracts 26(1-2):24.3). Nicot et al. teach a method of decreasing cell division by administering PACAP. Because PAC1 is the receptor for PACAP (specification, p. 5, last line), PACAP is a PAC1 ligand. Furthermore, Nicot et al. administered PACAP6-38, which applicant has acknowledged is an antagonist of the PAC1 receptor (specification, paragraph 0021, pp. 6 –7), and increased the proliferation of neuronal precursor cells, as indicated by the increased uptake of BrdU. The prior art teachings of Nicot et al. meet the limitations of claim 46.

13. Claim 46 is rejected under 35 U.S.C. 102(a) as being anticiapted by Suh et al. (2000. Society for Neuroscience Abstracts 26(1-2):311.15). Suh et al. teach that administration of PACAP decreases growth of neuronal precursors. Because PACAP is a PAC1 ligand, and because Suh et al. concluded from their experiments that PACAP "reduced precursor proliferation" after injection into the cerebral ventricle, the teachings of Suh et al. anticipate claim 46.

14. Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by DiCicco-Bloom et al. (1998. Annals of the New York Academy of Sciences 865:274-289), as evidenced by Alberts et al. The claim is drawn to a method of modulating the growth of a neuronal precursor cell by contacting said cell with a ligand of PACAP. DiCicco-Bloom et al. teach a method of contacting a culture of neuronal precursor cells with PACAP (see p. 278 – 280). The culture system of

DiCicco-Bloom et al. comprises neuronal precursor cells (see p. 277, final paragraph) and PACAP is a PAC1 ligand. The specification has not explicitly defined cell growth; the examiner has construed this term to include all of interphase cell division, as Alberts et al. (1994. Molecular Biology of the Cell; see particularly p. 865) teach that G1 and G2 are necessary for cell growth, and that the S phase, during which DNA is replicated, is a necessary step between G1 and G2. Furthermore, p. 881 of Alberts et al. teaches that a long interphase is necessary for cell growth. DiCicco-Bloom et al. teach that PACAP inhibits DNA synthesis (see paragraph spanning pp. 278 – 280). Because cell growth includes DNA synthesis, the prior art teachings anticipate all the limitations of this claim.

15. Claims 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Lu et al. (reference AZ on the information disclosure statement). Lu et al. teach that PACAP elicits a 43% decrease in ^{3}HdT incorporation into neuronal precursor cells 24 h after administration (p. 3359, first full paragraph). PACAP is a ligand for the PAC1 receptor. Furthermore, Lu et al. teach that a PAC1 ligand $PACAP_{6-38}$ elicits increases in proliferation of neuronal precursor cells (p. 3360, second column). The prior art teachings of Lu et al. anticipate claim 46.

16. Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Lu (1997. Ph.D. dissertation, January 1997). Lu teaches that administration of PACAP to neuronal precursor cells in vitro elicits a 43% reduction in ^{3}HdT incorporation into neuronal precursor cells 24 h after administration (p. 25). Lu also teaches that the ligand $PACAP_{6-38}$ inhibits PACAP-induced mitotic stimulation in sympathetic neuroblast cultures and increases proliferation of neuronal precursor cells in cortical cultures, and that this effect can be mimicked with a PACAP-specific antibody (pp. 29 – 30). The above teachings meet the limitations of claim 46. Furthermore, Lu teaches that both PACAP and the PAC1 receptor are expressed in embryos *in vivo* (p. 36) and suggests that the PACAP/PAC1 system promotes proliferation and differentiation *in vivo* (p. 37).

17. Claim 46 is rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The reasons why the teachings of Lu (1997) anticipate claim 46 are presented in the preceding paragraph. The face page of the document indicates that this is a dissertation submitted to Rutgers University, and that while it was written under the direction of inventor DiCicco-Bloom, the sole author is inventor Lu. The Rutgers University Catalog for the Graduate School at New Brunswick, covering the years 1997 – 1999 describes the dissertation as an original investigation. The first sentence under the heading "Dissertation and Dissertation Committee" on page 33 is particularly informative, as it states that "[e]ach candidate for the

doctorate pursues, under faculty direction, *an original investigation* of a problem or problems in a field of concentration and presents the results of the investigation in a dissertation" (emphasis added). This suggests that the subject matter in the dissertation was invented by Lu and not by any of the other inventors.

18. Claims 46 is rejected under 35 U.S.C. 102(e) as being anticipated by Moro et al. (U.S. Patent 6,017,533, reference AC on the information disclosure statement, issued 25 January 2000, filed 25 April 1996), as evidenced by Lu et al. (1997, reference AZ on the information disclosure statement). Moro et al. disclose several agents, including NSP, MAX, and M65 and their C-terminal amidized peptides, which are ligands of the PAC1 receptor (see column 3, lines 10 – 23). Moro et al. teach methods of administering the agents to mammals, thereby "expanding nervous processes" and "contracting nervous processes" (see column 4, lines 25 – 41). They further teach that MAX, MAX-NH_2, NSP, and NSP-NH_2 bind to the PAC1 receptor with high affinity (see column 6, first paragraph). Therefore these are ligands of PAC1. Moro et al. further teach methods of increasing and decreasing cAMP concentration in cells that express PAC1 receptors by administering their compounds (see column 4, lines 25 – 41). Lu et al. teach that the actions of the PAC1 receptors on proliferation are mediated by cAMP (see p. 3359, second column, third complete paragraph, and p. 3360, figure 4). Therefore the method of Moro et al., administration of PAC1 ligands to mammals, is inherently a method of modulating the growth of neuronal precursor cells, as it increases cAMP in cells which express PAC1, and Lu et al. teach that cAMP mimics the effects of PACAP in proliferating neuronal precursor cells, which express PAC1. The teachings of Moro et al. anticipate claim 46.

Conclusion

19. No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.
March 24, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
3-28-05